As cataloged in Applicants' initial response, the Examiner rejected claims 11-15 as allegedly obvious within the meaning of 35 U.S.C. § 103(a) over Kolterman *et al.*, *Diabetes Care*, vol. 18, no. 8 (1995), in view of Rosenbloom *et al.*, *Am. J. Dis. Child*, 131: 881-885 (1977), Rink *et al.*, *WO 92/20367*, and Morley *et al.*, *Am. J. Physiol.* 267:R178-R184 (1994). The Examiner pointed out that, "Kolterman *et al.* are silent about . . . the effect of amylin or amylin agonist on weight gain." Rosenbloom *et al.* – written over ten years before news of the discovery of amylin at Oxford University by Dr. Garth Cooper and Mr. Antony Willis was published in the August 1, 1987 edition of *The Lancet* – does not mention amylin or amylin agonists, and Rink *et al.* '367 teaches away from Applicants' claimed invention by reporting that treatment with amylin likely has no useful effect on weight reduction in an animal (Rink *et al.* '367, page 11).

This Supplemental Response is submitted to provide the Examiner with supplementary information in furtherance of Applicants' previous argument that the citation of Morley *et al.* (1994) does not save the rejection of claims 11-15. It also supports the withdrawal of the other rejections of claims 1-5, 6-8, 1 and 5, and 1-10 that were made by the Examiner. Morley *et al.* report the alleged modulation of food intake in mice with peripherally administered amylin. Although Morley *et al.* closes with the conclusion that, "[T]he answer to whether amylin is truly a physiological satiation agent will need to wait until amylin antagonists become available" (R183, col. 2, paragraph 2), the Examiner alleged that Morley *et al.* teach a method of "effectively suppressing or reducing food intake (i.e., treating obesity) . . . by administering up to 200 micrograms of amylin per kg." In other words, the Examiner equated the reduction of food intake with the treatment of obesity in support of her rejection.

The Declaration of Young submitted herewith describes the result of an animal study showing that the administration of amylin resulted in a dose dependent decrease in body weight in spite of the fact that there was no overall reduction in food intake. Thus, contrary to the assertion of the Examiner, this experiment indicates that food intake is not predictive of weight reduction. As previously argued, the Examiner's reliance on short-term, restricted studies relating to the alleged affect of amylin on food intake are not determinative and do not support the rejection of any of claims 1-15.

The Young Declaration is also relevant to Applicants' response (i) to the Examiner's rejection of claims 1 and 5 under 35 U.S.C. § 103(a) over Morley *et al.*, *Am. J. Physiol.* 267:R178-R184 (1994), (ii) to the rejection of claims 1-5 under 35 U.S.C. § 103 (a) as allegedly unpatentable over Arnelo *et al.*, *Am. J. Physiol.* 271:6 pt 2:R1654-R1659 (1996) (Arnelo I), or Arnelo *et al.*, *Scand J. Gastroenterol.* 31:83-89 (1996) (Arnelo II), and (iii) to the Examiner's rejection of claims 6-8 for alleged obviousness over Arnelo I or Arnelo II as applied to pending claim 5 in further view of Bennett *et al.* (U.S. Patent No. 5,955,433, "Method of Thrombin Inhibition"). As noted in Applicants' initial response, (i) Morley *et al.* actually teaches away from the claimed inventions because it showed that amylin treated mice ate for longer periods of time compared to saline treated controls ("Inspection of the data revealed that control mice decreased food consumption during this period, but amylin-treated mice continued to eat about the same amount as during the 0- to 30-min test period"; Morley *et al.*, R182, column 2 (emphasis added)), (ii) Arnelo I would not suggest to one of ordinary skill in the art any method of treating obesity in humans, as there was in fact no reported weight loss in Arnelo's experimental study on rats, and (iii) Arnelo II reported that, "Bolus injection or infusion of human IAPP did not inhibit food intake at any dose" and that suppression of feeding on

administration of rat IAPP bolus injection and infusion effects had vanished by 24 hours at the 5 and 10 nmol/kg doses (Arnelo II, page 85, last paragraph).[1]

Applicants submit that, when the art of the time is considered as a whole, there is plainly insufficient motivation to do what Applicants describe and claim. Viewed in its entirety, in light of the knowledge in the art, and in further view of the Young Declaration detailing the results of a study confirming that reduction of body weight cannot be predicted from food intake, the Morley *et al.* and Arnelo *et al.* data would not suggest to one of ordinary skill in the art at the time of filing the instant application that it would have been obvious to use an amylin or amylin agonist to treat or prevent obesity in humans. Applicants respectfully request that the rejections of claims 1-15 be reconsidered and withdrawn.

CONCLUSION

Applicants submit that the pending claims are in condition for allowance, and seek an early notice to that effect. Should the Examiner have any remaining questions, she is encouraged to telephone the undersigned so that they may be promptly resolved.

Respectfully submitted,

Dated: 10/22/01

By: _____
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[1] See Applicants' initial Response to Office Action regarding the presumption by the Examiner that reference to IAPP is equivalent to a reference to amylin.